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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/059,447	01/29/2002	Daniel S. Smith	0994.00134	8310

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KOHN & ASSOCIATES
Suite 410
30500 Northwestern Highway
Farmington Hills, MI 48334

EXAMINER

RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/059,447

Applicant(s)

SMITH, DANIEL S.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 December 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 5-8 and 10-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12-28-04 has been entered.

Claims 1-12 are currently pending and are present for examination. Claims 1-4 and 9 are now under consideration. Claims 5-8, 10-12 remain withdrawn from consideration as being drawn to non-elected invention.

Applicants' amendments and arguments filed on 12-28-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically, Examiner has withdrawn the previously held rejections under 35 U.S.C. 112, 2nd paragraph in view of claim amendments. Without acquiescing with applicant's arguments Examiner has withdrawn the rejection under 35 U.S.C. 102/103.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

It is noted that applicants have filed a set of colored drawings. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37

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CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Sequence Compliance

Applicant's amendment to specification complying with Sequence rules is noted and entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a single purified α -N-acetyl-D-galactosaminidase (NAG) purified from *C.perfringens* comprising the full length amino acid sequence SEQ ID NO:11, does not reasonably provide enablement for any variants or mutants (functional or structural) of

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SEQ ID NO:11 having the peptide sequences set forth in SEQ ID NO:1-10 or functional analogs of the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-4 and 9 are so broad as to encompass any NAG including variants, mutants and recombinants of SEQ ID NO:11 or those comprising amino acid fragments SEQ ID NO:1-10 from any source. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number NAG broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the single purified NAG. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use of the full length SEQ ID

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NO: 11 as NAG but provides no guidance with regard to the making of variants and mutants of the same or variants or mutants of NAGs comprising amino acid sequences SEQ ID NO:1-10 or with regard to other uses. Furthermore as SEQ ID NO 1-10 comprise very short amino acid sequences, those skilled in the art need to be provided highly specific guidance for making variants comprising said sequences. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim. It should also be noted here that amino acid sequences that were found to be at least 90% homologous with, for example SEQ ID NO:6 had entirely a different function than that of NAG (see enclosed sequence alignment at the end of this Office action).

While enzyme isolation, recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

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The specification does not support the broad scope of the claims which encompass all modifications to any NAG because the specification does not establish: (A) first of all the full length amino acid sequence of the enzymes comprising SEQ ID NO:1-10; (B) regions or specific amino acids of the protein structure which may be modified without affecting NAG activity; (B) the general tolerance of NAGs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including homologs and functional analogs of *C.perfringens* NAG. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of NAGs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicant submits that claims are now amended to more specifically recite the sequence must be selected from the group of 1-11 and therefore claims are enabled. Examiner respectfully disagrees that such an amendment completely overcome the enablement issues in the above claims. Claims are still directed to polypeptides comprising short peptide sequences wherein the structure of major portion of the full length polypeptides are unknown. Furthermore, claim 9 continues to be directed to functional analogs

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which in other words comprise variants or mutants for which applicants provide no guidance for making them. While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants i.e., variants based on very short stretches of amino acids, requires that one of ordinary skill in the art know or be provided with guidance for the selection of specific amino acid residues that can be modified and which of the infinite number of variants have the claimed property along with amino acid sequence of the full length polypeptide. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting activity; (B) the general tolerance of -NAGs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Therefore the above rejection is maintained.

Claims 1-4 and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of NAG comprising specific 8-25 amino acid long peptide sequences and functional analogs of the same. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the isolation and characterization of only a single species of NAG, i.e., that from *C.perfringens* having the amino acid sequence SEQ ID NO:11. Moreover, the specification fails to describe any other representative species by sufficient identifying characteristics or properties to show that applicant was in possession of the claimed genus. The identifying characteristics recited in Claims 1, 4 and 9, i.e., enzymatic activity, approximate molecular weight, and the 5 peptide sequences which together include just a partial structural description of the structure of the single disclosed species, do not include sufficient characteristics to limit the claimed genus to proteins which are not highly variable in both structure and function. The claims include species in which a significant per cent of the amino

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acid sequence of the single disclosed species has been substituted. Therefore, the species within the genus are highly variable in structure. While Claim 3 adds two additional characteristic to the limitations of the genus of each of these claims, none of these characteristics, by itself is sufficient to change the fact that the claims include proteins which are highly variable in both structures. Thus for all the reasons discussed, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention. Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicant submits that claims have been amended to remove the language related to homologs and therefore the rejection should be withdrawn. Examiner respectfully disagrees with the applicant. Examiner also notes that applicant has not addressed the portion of the rejection directed at the claiming of enzymes whose only structure described is short amino acid sequences. Therefore the above rejection is maintained.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura

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Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

A handwritten signature in black ink, appearing to read 'Manjunath N. Rao', with a stylized flourish at the end.

Manjunath N. Rao, Ph.D.
Primary Examiner
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March 9, 2005